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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	19

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/126,945	Libermann et al.
Examiner	**Group Art Unit**
Scott D. Priebe, Ph.D.	1632

X Responsive to communication(s) filed on *Apr 5, 1999*.

X This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *24-100 and 105-148* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

X Claim(s) *84-100* is/are allowed.

X Claim(s) *24-26, 28, 29, 31, 32, 34, 35, 37, 38, 40-53, 55, 56, 58, 59, 61, 62, 64* is/are rejected.

X Claim(s) *27, 30, 33, 36, 39, 54, 57, 60, 63, 66, 110, and 112* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

The amendments filed 7/17/00 have been entered. Claims 11-16, 19, 101-104 have been cancelled. Claims 46, 48, 70, 72, 75, 79, 81, 84, 105-108, 116, 118, 121, 125, 127, 128, 132 and 134 have been amended. Claims 137-148 have been added. Claims 24-100 and 105-148 are pending.

The 4 sheets of Table I filed with the original application have been inserted into the specification as page numbers 103-106, and original pages 103-107 have been renumbered accordingly. However, the amendment (at page 9) indicates that there should be 5 pages to Table I to be inserted as pages 103-107. The transmittal letter filed with the application indicates that 14 sheets of drawings were filed, 10 of which correspond to Figures 1A-C and 2-10 and therefore 4 sheets of Table I . Clarification is requested.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The amendment to the paper copy of the "Sequence Listing" does not comply with 37 CFR 1.825(b) which requires a

substitute copy of the computer readable form of the "Sequence Listing" which incorporates the changes made to the paper copy.

Applicants are required to comply with all of the requirements of 37 C.F.R. §§ 1.821 through 1.825. *Any* response to this Office Action which fails to meet *all* of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. §§ 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

Claim Objections

Claim 121 is objected to because of the following informalities: The semicolon in line 2 is improper grammar, and should be deleted. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 137-148 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 137-148 are directed to polynucleotides comprising a nucleic acid, which encodes one of the recited epitopes of PDEF, fused to a nucleotide sequence heterologous to SEQ ID NO: 1. Page 25, lines 10-16, which only discloses the epitopes, is alleged to provide support for this embodiment. Starting at line 28 of page 25, the specification discloses fusion proteins comprising epitopes of PDEF as epitope tags. However, there is no apparent support for the generic embodiment instantly claimed with respect to "nucleotide sequence heterologous to SEQ ID NO: 1" in the context of a fusion to nucleic acid encoding an epitope of PDEF. There is no evidence of record that such a generic embodiment was contemplated by the inventors at the time the invention was made.

Claims 75-83 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 3/16/00 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims, as amended are directed to polynucleotides encoding a polypeptide that is a fragment of SEQ ID NO: 2 (or by the corresponding clone) that regulates "prostate-specific epithelial gene expression", and methods and products for making such a polypeptide.

The specification as originally filed provides no clear support for fragments that regulate generic "prostate-specific epithelial gene expression". The specification discloses only that PDEF

regulates expression of the Prostate-specific Antigen (PSA) gene, and does not disclose any other genes or genera of genes regulated by PDEF. It further discloses that PDEF gene expression is highly specific, primarily to the prostate. The specification provides only an assay for determining function of a given PDEF polypeptide with respect to regulation of PSA gene expression. In addition, there is no evidence of record that any and all genes expressed specifically in prostate epithelial cells share any common regulatory controls, or that regulation of the PSA gene shares any common regulatory features with any other genes expressed in prostate epithelial cells. Thus, there is no evidence of record that applicants were in possession, when the instant application was filed, of the invention that is now being claimed. These claims should be limited to fragments that regulate expression of the Prostate-specific Antigen gene.

Applicant's arguments filed 7/17/00 have been fully considered but they are not persuasive. At page 9, lines 1-5, the specification states "PDEF may also regulate epithelial specific gene expression". This speculation is not supported by any factual evidence presented in the specification, which discloses only that PDEF regulates the PSA gene. The fact that the specification explicitly presents such a speculation is a tacit admission that Applicant was not in possession of PDEF fragments that regulate "prostate-specific epithelial gene expression" in general, as opposed to those fragments that would regulate PSA gene expression. Page 36, lines 25-28 (and page 50, lines 22-25) of the specification indicates only that PDEF is primarily expressed in prostate, it does not identify any "prostate-specific epithelial gene expression" mediated by PDEF. While the specification as originally filed supports possession of the narrower

claimed embodiment of nucleic acids encoding PDEF fragments that would regulate PSA gene expression specifically, there is no evidence of possession (or even contemplation) of PDEF fragments that would regulate "prostate-specific epithelial gene expression" generally.

Claims 24-26, 28, 29, 31, 32, 34, 35, 37, 38, 40, 41, 43-53, 55, 56, 58, 59, 61, 62, 64, 65, 67-74, 105, 107, 109, 111, and 113-120 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 3/16/00, because the specification, while being enabling for a "nucleic acid" that encodes SEQ ID NO: 2 or a fragment of SEQ ID NO: 2 (as recited in the claims), does not reasonably provide enablement for polynucleotides that do not encode SEQ ID NO: 2 or a recited fragment of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicant's arguments filed 7/17/00 have been fully considered but they are not persuasive. With respect to disclosed utilities, the rejection clearly states that require that either the polynucleotide will hybridize with a PDEF nucleic acid or that it encode a polypeptide, either with PDEF function or that can be used to make antibodies that will be specific for a PDEF protein. All disclosed utilities enumerated in Applicant's arguments require polynucleotides with one of these properties. The specific uses which exploit one of these properties substantiate the basis of the rejection. For example, the only disclosed target for hybridization, whether it occurs in a priming reaction, *in situ* hybridization, triple helix formation or antisense binding, is a polynucleotide

comprising SEQ ID NO: 1. The vast majority of polynucleotides embraced by the claims would be inoperative for this utility for the reasons given. The specification fails to disclose any other targets for hybridization using polynucleotide probes, primers, or triple helix or antisense oligonucleotides whose nucleotide sequence differs from SEQ ID NO: 1. Applicant asserts that a single utility is all that is required to satisfy 35 USC 112, citing *Raytheon Co. v. Roper Corp.* This is an over-generalization. To satisfy 35 USC 112, first para., the claims must also be commensurate in scope with the enabling disclosure (see MPEP 2164.08), which they are not for the reasons of record. As explained in the rejection, a polynucleotide that encodes SEQ ID NO: 2 embraces polynucleotides that have as low as 65% identity to SEQ ID NO: 1 due to the degeneracy of the genetic code. As explained, such polynucleotides would not hybridize to SEQ ID NO: 1 under any conditions, and the specification does not disclose alternative targets for hybridization for such polynucleotides, whether as a probe or primer.

While the specification identifies useful epitopes from PDEF (SEQ ID NO: 2) the claims are not limited to polynucleotides that encode polypeptides comprising or consisting of one of these epitopes. In many cases, a single amino acid substitution in one of these epitopes would be sufficient to yield an antibody (directed to the modified amino acid sequence - a new epitope) that would not bind specifically to the unmodified, original epitope. Also, even if a polypeptide comprised an unaltered epitope, extensive changes in amino acid sequence embraced by the claims would lead to other new epitopes, which in turn would yield antibodies that would not bind to the corresponding unmodified amino acid sequence. Thus, while a polyclonal antisera raised against a

protein 90% identical to SEQ ID NO: 2 may contain some antibodies that would bind to PDEF, it would also contain many antibodies that would not. The specification provides no utility (i.e. does not teach how to use) for such a mixed polyclonal antisera. It is not clear how *In re Angstadt* applies to this situation. One can envision polynucleotides that meet the structural limitations of the claims. However, the claims fail to meet 35 USC 112, first para. because one cannot predict or identify, without undue experimentation, those relatively few embodiments of all those embraced by the claims which would be inoperative for the utilities disclosed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43, 67, 76, 113, 122 and 129 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically for recitation of "heterologous polynucleotide", for the reasons of record set forth in the Office action of 3/16/00.

Applicant's arguments filed 7/17/00 have been fully considered but they are not persuasive. The term "heterologous" is not defined in the specification. The use of "heterologous" in the context of fusion proteins clearly does not apply to the instant claims. The claims do not recite any fusion polypeptide nor does the discussion of fusion polypeptides in the specification make any mention of polynucleotides. Thus, Applicant's explanation clearly takes the use of

"heterologous", as applied to fusion proteins, out of context. Claims 46, 48, 49, 70, 72, 73, 81, 82, 116, 118, 119, 125, 127, 132, 134 and 135 as amended are definite because the claim now provides a context, i.e. relative to "the first nucleic acid", for determining the meaning of "heterologous regulatory sequence", i.e. it is not a regulatory sequence of the PDEF gene.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

It is noted that "nucleic acid encoding an amino acid sequence" is interpreted as being open, i.e. the nucleic acid may encode an amino acid sequence comprising the recited amino acid sequence. With respect to claims 128-136, it is noted that any polypeptide comprising a single dipeptide present in SEQ ID NO: 2 between positions 14-277 meets the limitations of the polypeptide recited in the claims, where n - m = 1. For example, a PA dipeptide appears at amino acid positions 48-49 and 298-299 of SEQ ID NO: 2, and a KL dipeptide appears at amino acid positions 139-140 and 304-305 of SEQ ID NO: 2.

Claims 105-106, 113-118, and 120-148 are rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Acc. No. AA662204 (Ref. AT-8 filed 2/11/99).

GenBank Acc. No. AA662204 discloses a isolated polynucleotide, plasmid vector (having heterologous promoters operably linked to the insert) and cell where the polynucleotide (514 nucleotides in length) comprises a nucleic acid, nucleotides 3-181, that is identical to nucleotides 1242-1420 of SEQ ID NO: 1 and that encodes 59 amino acids (amino acids 277-335) of SEQ ID NO: 2. Thus this nucleic acid is 99.4% identical to nucleotides 276-335 of SEQ ID NO: 1, which encodes 60 amino acids of SEQ ID NO: 2. The polynucleotide from positions 3-514 differs from nucleotides 1242-1753 of SEQ ID NO: 1 by only two nucleotides (at positions 1432 and 1440). The

With respect to claims 121-127, the prior art plasmid vector containing the disclosed sequence meets the limitations of the claims. The prior art vector, being much larger than 600 nucleotides, contains a first nucleic acid at least 600 nucleotides long comprising the insert (or part of the insert) which would hybridize to SEQ ID NO: 1 or the cloned cDNA under the conditions recited. The rejection of claims 121-127 could be overcome by inserting --over the entire length of the first nucleic acid-- before "to a second nucleic acid".

With respect to claims 128-136, the prior art polynucleotide includes codons for the PA and KL dipeptides corresponding to SEQ ID NO: 2 positions 298-299 and 304-304, respectively, mentioned above, which anticipates the claims when m and n are either 48 and 49, respectively, or 139 and 140, respectively.

Claims 128-137, 140, 142-146 and 148 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (Dev. Biol. 151: 176-191, 1992).

Chen et al. disclose an isolated polynucleotide that encodes the *Drosophila* ets-4 polypeptide (page 182, Fig. 2C). Amino acids 71-94 of ets-4 are identical to amino acids 294-317 of instant SEQ ID NO: 2. Chen et al. discloses vectors comprising the polynucleotide, where a heterologous promoter is operably linked to the insert, and cells comprising the vectors (page 178 through page 179, col. 1).

With respect to claims 128-136, the prior art polynucleotide includes the codons for the PA and KL dipeptides corresponding to SEQ ID NO: 2 positions 298-299 and 304-304, respectively, mentioned above, which anticipates the claims when m and n are either 48 and 49, respectively, or 139 and 140, respectively.

Double Patenting

Applicant remains advised that should claims 27, 30, 33, 36 and 39 be found allowable, claims 54, 57, 60, 63 and 66 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant's arguments filed 7/17/00 have been fully considered but they are not persuasive. The scope of claims 27, 30, 33, 36, 39, 54, 57, 60, 63 and 66 does not embrace either all polynucleotides comprising an a nucleic acid that is "90% identical" to a reference polynucleotide or all that encode a polypeptide "90% identical" to a reference amino acid sequence. The claims are limited to polynucleotides that comprise a nucleic acid that specifically encodes one of the amino acid sequences recited in parts (a)-(e) of claims 24 or 51. Despite the fact that independent claims 24 and 51 have different scopes, the corresponding dependent claims have the same scope.

Allowable Subject Matter

Claims 27, 30, 33, 36, 39, 54, 57, 60, 63, 66, 108, 110 and 112 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 84-100 are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen M. Hauda, can be reached on (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott D Priebe

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